

Synthesis, Structural Investigations, Hydrogen-Deuterium Exchange Studies and Molecular Modeling of Conformationally Stabilized Aromatic Oligoamides

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Synthetic Procedures/Characterizations

All the reagents were obtained from commercial suppliers and used as received unless otherwise noted. Aqueous solutions were prepared from distilled water. The organic solutions from all liquid extractions were dried over anhydrous Na_2SO_4 for a minimum of 15 minutes before filtration. Reactions were monitored by thin-layer chromatography (TLC) on silica gel pre-coated glass plate (0.225 mm thickness, 60F-254, E. Merck). Flash column chromatography was performed using pre-coated 0.2 mm silica plates from Selecto Scientific. Chemical yields refer to pure isolated substances. ^1H and ^{13}C NMR spectra were recorded on either a Bruker ACF-300 or AVF-500 spectrometer. In addition, key compounds were characterized by 2D NOSEY and/or X-ray Diffraction. ^1H NMR spectra were recorded on Bruker ACF300 (300 MHz) and ACF500 spectrometers (500 MHz). The solvent signal of CDCl_3 was referenced at $\delta = 7.26$, and $\text{DMSO}-d_6$ at 2.50. Coupling constants (J values) are reported in Hertz (Hz). ^1H NMR data are recorded in the order: chemical shift value, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), number of protons that gave rise to the signal and coupling constant, where applicable. ^{13}C Spectra are proton-decoupled and recorded on Bruker ACF300 (300 MHz) and ACF500 spectrometers (500 MHz). The solvent, CDCl_3 was referenced at $\delta = 77$ ppm and $\text{DMSO}-d_6$ at 39.5 ppm. CDCl_3 (99.8% deuterated) was purchased from Aldrich and used without further purification.

Compound 1a: 2,5-dihydroxybenzoic acid (4.62 g, 30.0 mmol) was dissolved in MeOH (60 mL), to which concentrated H_2SO_4 (5 mL) was added. The mixture was heated under reflux for 48 hrs. The solvent was then removed *in vacuo* and the residue was dissolved in CH_2Cl_2 (100 mL), washed with water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the pure product **1a** as a light brown solid. Yield: 4.89 g, 97%. ^1H NMR (300 MHz, CDCl_3) δ 10.33 (s, 1H), 7.28 (d, 1H, $J = 3.1$), 7.01 (d, 1H, $J = 8.9$), 6.88 (d, 1H, $J = 8.9$), 4.76 (s, 1H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.89, 156.12, 148.52, 124.85, 119.09, 115.55, 112.87, 53.08. HRMS-ESI: calculated for $[\text{M}]^+$ ($\text{C}_8\text{H}_8\text{O}_4$): m/z 167.0344 found: m/z 167.0343.

Compound 1b: **1a** (1.34 g, 8.00 mmol) was dissolved in anhydrous acetone (30 mL), to which anhydrous K_2CO_3 (2.00 g, 14.5 mmol) and iodomethane (0.50 mL, 8.00 mmol) was added. The mixture was heated under reflux for 48 hrs. The reaction mixture was then filtered and the solvent was removed *in vacuo*. The concentrate was dissolved in CH_2Cl_2 (100 mL), washed with water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the crude product, which was purified by flash column chromatography (silica gel) using hexane/ethyl acetate (4:1 v/v) as the eluent to give pure product **1b** as a yellow liquid. Yield: 0.95 g, 65%. ^1H NMR (300 MHz, CDCl_3) δ 10.33 (s, 1H), 7.07 (d, 1H, $J = 3.2$), 7.04 (d, 1H, $J = 3.2$), 6.90 (d, 1H, $J = 5.9$), 3.92 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.60, 156.41, 152.35, 124.21, 118.74, 112.12, 60.64, 55.94, 52.50. HRMS-ESI: calculated for $[\text{M}]^+$ ($\text{C}_9\text{H}_{10}\text{O}_4$): m/z 181.0579 found: m/z 181.0579.

Compound 1c: **1a** (1.34 g, 8.00 mmol) was dissolved in anhydrous acetone (30 mL), to which anhydrous K_2CO_3 (2.00 g, 14.5 mmol) and 1-bromooctane (1.38 mL, 8.00 mmol) was added. The mixture was heated under reflux for 48 hrs. The reaction mixture was then filtered and the solvent was removed *in vacuo*. The concentrate was dissolved in CH_2Cl_2 (40 mL), washed with water (2 x 30 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the crude product, which was recrystallized from MeOH to give pure product **1c** as a light yellow solid. Yield: 1.57 g, 70%. ^1H NMR (300 MHz, CDCl_3) δ 10.35 (s, 1H), 7.29 (d,

1H, $J = 3.1$), 7.08 (d, 1H, $J = 9.0$), 6.90 (d, 1H, $J = 9.0$), 3.95 (s, 3H), 3.88 (m, 2H), 1.76 (m, 2H), 1.42 (m, 2H), 1.25 (m, 8H), 0.89 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 171.02, 156.63, 152.24, 125.25, 119.10, 113.57, 112.53, 69.51, 52.92, 32.49, 30.03, 29.97, 29.91, 26.71, 23.33, 14.76. HRMS-EI: calculated for $[\text{M}]^+$ ($\text{C}_{16}\text{H}_{24}\text{O}_4$): m/z 280.1675 found: m/z 280.1677.

Compound 1d: 1a (1.34 g, 8.00 mmol) was dissolved in anhydrous acetone (30 mL), to which anhydrous K_2CO_3 (2.00 g, 14.5 mmol) and 2-bromopropane (3.80 mL, 8.00 mmol) was added. The mixture was heated under reflux for 48 hrs. The reaction mixture was then filtered and the solvent was removed in *vacuo*. The concentrate was dissolved in CH_2Cl_2 (40 mL), washed with water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the crude product, which was purified by flash column chromatography (silica gel) using hexane/ethyl acetate (4:1 v/v) as the eluent to give pure product **1d** as a yellow liquid. Yield: 0.86 g, 51%. ^1H NMR (300 MHz, CDCl_3) δ 10.33 (s, 1H), 7.28 (d, 1H, $J = 3.1$), 7.02 (d, 1H, $J = 5.3$), 6.86 (d, 1H, $J = 5.3$), 4.38 (m, 1H), 3.89 (s, 3H) 1.31 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3) δ 170.86, 156.66, 150.67, 126.71, 118.94, 116.18, 112.59, 71.82, 52.79, 22.51. HRMS-EI: calculated for $[\text{M}]^+$ ($\text{C}_{11}\text{H}_{14}\text{O}_4$): m/z 210.0892 found: m/z 210.0893.

Compound 1e: 1b (0.18 g, 1.00 mmol) and Montmorillonite K10 (0.50 g) were added to a suspension of bismuth nitrate (0.39 g, 1.00 mmol) in THF (10 mL). The mixture was stirred at room temperature for 1 h and solid was filtered. Solvent was then removed in *vacuo* and the residue was dissolved in CH_2Cl_2 . The filtrate was washed with 1M HCl (1 x 50 mL), water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the pure product **1e** as a yellow solid. Yield: 0.14 g, 63%. ^1H NMR (300 MHz, CDCl_3) δ 11.46 (s, 1H), 7.72 (d, 1H, $J = 7.9$), 7.70 (d, 1H, $J = 7.9$), 4.01 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 169.28, 151.37, 150.51, 138.27, 122.42, 117.12, 68.61, 56.95, 53.82. HRMS-ESI: calculated for $[\text{M}]^-$ ($\text{C}_9\text{H}_9\text{NO}_6$): m/z 226.0352 found: m/z 226.0364.

Compound 1f: 1c (0.28 g, 1.00 mmol) and Montmorillonite K10 (0.50 g) were added to a suspension of bismuth nitrate (0.39 g, 1.00 mmol) in THF (10 mL). The mixture was stirred at room temperature for 1 h and solid was filtered. Solvent was then removed in *vacuo* and the residue was dissolved in CH_2Cl_2 . The filtrate was washed with 1M HCl (1 x 50 mL), water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the crude product, which was recrystallized from MeOH to give pure product **1f** as a yellow solid. Yield: 0.19 g, 58%. ^1H NMR (300 MHz, CDCl_3) δ 11.44 (s, 1H), 7.72 (d, 1H, $J = 3.3$), 7.69 (d, 1H, $J = 3.1$), 4.00 (s, 3H), 3.96 (m, 2H), 1.79 (m, 2H), 1.31 (m, 2H), 1.29 (m, 8H), 0.89 (m, 3H). ^{13}C NMR (75 MHz, CDCl_3) δ 169.30, 150.90, 150.33, 138.19, 122.97, 117.68, 116.85, 69.95, 53.73, 32.40, 29.88, 29.81, 29.64, 26.52, 23.26, 14.68. HRMS-ESI: calculated for $[\text{M}]^+$ ($\text{C}_{16}\text{H}_{23}\text{NO}_6$): m/z 324.1447 found: m/z 324.1461.

Compound 1g: 1d (0.21 g, 1.00 mmol) and Montmorillonite K10 (0.50 g) were added to a suspension of bismuth nitrate (0.39 g, 1.00 mmol) in THF (10 mL). The mixture was stirred at room temperature for 1 h and solid was filtered. Solvent was then removed in *vacuo* and the residue was dissolved in CH_2Cl_2 . The filtrate was washed with 1M HCl (1 x 50 mL), water (2 x 50 mL) and dried over anhydrous Na_2SO_4 . Removal of CH_2Cl_2 gave the pure product **1g** as a yellow liquid. Yield: 0.17 g, 67%. ^1H NMR (300 MHz, CDCl_3) δ 11.44 (s, 1H), 7.68 (d, 1H, $J = 3.1$), 7.66 (d, 1H, $J = 3.1$), 4.49 (m, 1H), 3.97 (s, 3H), 1.41 (s, 6H). ^{13}C NMR (75

MHz, CDCl₃) δ 169.24, 150.35, 149.50, 124.63, 122.31, 119.37, 118.16, 72.43, 53.67, 22.42. HRMS-ESI: calculated for [M]⁺(C₁₁H₁₃NO₆): m/z 254.0665 found: m/z 255.0660.

Compound 1h: 1e (2.27 g, 10.0 mmol) was dissolved in anhydrous DMF (30 mL), to which anhydrous K₂CO₃ (4.00 g, 25.0 mmol) and iodomethane (0.75 mL, 12.0 mmol) was added. The mixture was heated under reflux for 60 °C hrs. CH₂Cl₂ (100 mL) was then added and the reaction mixture was filtered. The solvent was removed in *vacuo* and the concentrate was dissolved in CH₂Cl₂ (100 mL), washed with water (2 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the pure product **1h** as a red solid. Yield: 2.19 g, 91%. ¹H NMR (300 MHz, CDCl₃) δ 7.54 (s, 1H), 7.42 (s, 1H), 3.94 (s, 6H), 3.86 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.38, 155.41, 147.39, 146.37, 128.78, 121.66, 114.21, 65.01, 56.90, 53.48. HRMS-EI: calculated for [M]⁺(C₁₀H₁₁NO₆): m/z 241.0586 found: m/z 241.0587.

Compound 1i: 1f (3.25 g, 10.0 mmol) was dissolved in anhydrous DMF (30 mL), to which anhydrous K₂CO₃ (4.00 g, 25.0 mmol) and iodomethane (0.75 mL, 12.0 mmol) was added. The mixture was heated under 60 °C for 4 hrs. CH₂Cl₂ (100 mL) was then added and the reaction mixture was filtered. The solvent was removed in *vacuo* and the concentrate was dissolved in CH₂Cl₂ (100 mL), washed with water (3 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the crude product, which was recrystallized from MeOH to give pure product **1i** as a yellow solid. Yield: 2.44 g, 72%. ¹H NMR (300 MHz, CDCl₃) δ 7.52 (d, 1H, J = 3.3), 7.40 (d, 1H, J = 3.1), 3.93 (m, 2H), 3.92 (s, 3H), 3.61 (s, 3H), 1.77 (m, 2H), 1.43 (m, 2H), 1.27 (m, 8H), 0.86 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 166.09, 150.52, 149.97, 134.44, 121.35, 115.16, 114.63, 68.91, 54.81, 51.57, 31.81, 29.64, 29.37, 28.95, 25.96, 22.83, 14.06. HRMS-ESI: calculated for [M]⁺(C₁₇H₂₅NO₆): m/z 339.1682 found: m/z 339.1691.

Compound 1j: 1g (2.55 g, 10.0 mmol) was dissolved in anhydrous DMF (30 mL), to which anhydrous K₂CO₃ (4.00 g, 25.0 mmol) and iodomethane (0.75 mL, 12.0 mmol) was added. The mixture was heated under 60 °C for 4 hrs. CH₂Cl₂ (100 mL) was then added and the reaction mixture was filtered. The solvent was removed in *vacuo* and the concentrate was dissolved in CH₂Cl₂ (100 mL), washed with water (2 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the pure product **1j** as a red liquid. Yield: 2.19 g, 81%. ¹H NMR (300 MHz, CDCl₃) δ 7.52 (d, 1H, J = 3.2), 7.39 (d, 1H, J = 3.2), 4.55 (m, 1H), 3.94 (s, 6H), 1.36 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 165.48, 153.81, 147.12, 146.40, 128.72, 123.45, 115.93, 72.20, 65.01, 53.47, 22.82. HRMS-EI: calculated for [M]⁺(C₁₂H₁₅NO₆): m/z 269.0899 found: m/z 269.0902.

Compound 1k: 1h (1.25 g, 5.20 mmol) was dissolved in hot MeOH (20 mL), to which 1N NaOH (10 mL, 10.0 mmol) was added. The mixture was heated under reflux for 1 h and then more water (50 mL) was added. The aqueous layer was neutralized by addition of 1M HCl (15 mL). The precipitated crude product was collected by filtration, which was recrystallized from MeOH to give a yellow solid **1k**. Yield: 0.63 g, 53%. ¹H NMR (300 MHz, CDCl₃) δ 13.61 (s, 1H), 7.66 (d, 1H, J = 3.3), 7.51 (d, 1H, J = 3.3), 3.84 (s, 3H), 3.82 (s, 3H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 165.32, 154.47, 145.58, 144.57, 129.01, 120.05, 112.45, 63.81, 56.33. HRMS-ESI: calculated for [M]⁺(C₉H₉NO₆): m/z 226.0352 found: m/z 226.0346.

Compound 1l: 1i (2.80 g, 8.30 mmol) was dissolved in hot MeOH (30 mL), to which 1N NaOH (17 mL, 17.0 mmol) was added. The mixture was heated under reflux for 1 h and then quenched with water (100 mL).

The aqueous layer was neutralized by addition of 1M HCl (25 mL). The precipitated crude product was collected by filtration, which was recrystallized from MeOH to give a yellow solid **1l**. Yield: 2.30 g, 85%. ¹H NMR (300 MHz, CDCl₃) δ 13.67 (s, 1H), 7.65 (d, 1H, *J* = 3.2), 7.53 (d, 1H, *J* = 3.1), 3.92 (m, 2H), 3.59 (s, 3H), 1.70 (m, 2H), 1.40 (m, 2H), 1.19 (m, 8H), 0.79 (m, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.44, 154.92, 146.40, 144.78, 125.81, 122.18, 116.07, 69.41, 64.78, 31.76, 29.21, 29.16, 28.89, 25.85, 22.62, 14.06. HRMS-EI: calculated for [M]⁺ (C₁₆H₂₃NO₆): *m/z* 324.1447 found: *m/z* 324.1453.

Compound 1m: 1j (2.69 g, 10.0 mmol) was dissolved in hot MeOH (40 mL), to which 1N NaOH (20 mL, 20.0 mmol) was added. The mixture was heated under reflux for 1h and then more water (100 mL) was added. The aqueous layer was neutralized by addition of 1M HCl (30 mL). The precipitated crude product was collected by filtration, which was recrystallized from MeOH to give a yellow solid **1m**. Yield: 1.68 g, 66%. ¹H NMR (300 MHz, CDCl₃) δ 7.78 (d, 1H, *J* = 3.2), 7.54 (d, 1H, *J* = 3.2), 4.60 (m, 1H), 4.02 (s, 3H), 1.38 (s, 6H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 165.38, 152.69, 145.72, 144.37, 129.08, 121.60, 113.95, 71.02, 63.79, 21.47. HRMS-ESI: calculated for [M]⁺ (C₁₁H₁₃NO₆): *m/z* 254.0665 found: *m/z* 254.0659.

Compound 1o: 2-hydroxy-5-methylbenzoic acid (2.00 g, 13.0 mmol) was dissolved in MeOH (40 mL), to which concentrated H₂SO₄ (5 mL) was added. The mixture was heated under reflux for 48 hrs. The solvent was then removed in *vacuo* and the residue was dissolved in CH₂Cl₂ (100 mL), washed with water (2 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the pure ester which could directly used for the next step. The ester (0.17 g, 1.00 mmol) was dissolved in 20ml CH₂Cl₂ to which concentrated (69%) HNO₃ (0.10 mL, 1.56 mmol) was added with stirring at -20 °C. Concentrated (95%) H₂SO₄ (0.20 mL, 2.74 mmol) was then added dropwise to the reaction mixture. After 20 min, the reaction was quenched with 50 mL of distilled water. The CH₂Cl₂ layer was washed with water (2 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the pure product **1o** as a yellow solid. Yield: 1.00 g, 80%. ¹H NMR (300 MHz, CDCl₃) δ 11.74 (s, 1H), 7.98 (s, 1H), 7.95 (s, 1H), 4.00 (s, 1H), 2.37 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 169.76, 154.29, 147.91, 136.95, 135.21, 132.26, 129.00, 53.71, 20.86. HRMS-ESI: calculated for [M]⁺ (C₉H₉NO₅): *m/z* 210.0402 found: *m/z* 210.0404.

Compound 1p: 1o (1.00 g, 4.73 mmol) was dissolved in anhydrous DMF (15 mL), to which anhydrous K₂CO₃ (2.60 g, 19.0 mmol) and iodomethane (0.75 mL, 12.0 mmol) was added. The mixture was heated under 60 °C for 4 hrs. CH₂Cl₂ (50 mL) was then added and the reaction mixture was filtered. The solvent was removed in *vacuo* and the concentrate was dissolved in CH₂Cl₂ (50 mL), washed with water (2 x 50 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave the pure product as white solid **1p**. Yield: 1.01 g, 83%. ¹H NMR (300 MHz, CDCl₃) δ 7.82 (s, 1H), 7.71 (s, 1H), 3.96 (s, 3H), 3.95 (s, 3H), 2.40 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.72, 151.75, 145.83, 136.72, 134.84, 129.33, 127.72, 64.92, 53.41, 21.20. HRMS-ESI: calculated for [M]⁺ (C₁₀H₁₁NO₅): *m/z* 224.0553 found: *m/z* 224.0550.

Compound 1q: 1p (1.00 g, 4.40 mmol) was dissolved in hot MeOH (20 mL), to which 1N NaOH (10 mL, 10.0 mmol) was added. The mixture was heated under reflux for 1 h and then more water (50 mL) was added. The aqueous layer was neutralized by addition of 1M HCl (15 mL). The precipitated crude product was collected by filtration, which was recrystallized from MeOH to give a white solid **1q**. Yield: 0.51 g, 59%. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.89 (s, 1H), 7.83 (s, 1H), 3.84 (s, 3H), 2.36 (s, 3H). ¹³C NMR (125 MHz,

DMSO-*d*₆) δ 165.64, 149.20, 144.75, 135.29, 134.36, 127.72, 127.58, 63.64, 19.75. HRMS-ESI: calculated for [M]⁺ (C₉H₉NO₅): *m/z* 210.0402 found: *m/z* 210.0400.

Compound 1r: Salicylic acid (10.0 g, 72.5 mmol) was dissolved in 200 mL of CH₂Cl₂, to which concentrated HNO₃ (69%, 6.05 mL, 94.2 mmol) was added with stirring at 0 °C. Concentrated H₂SO₄ (95%, 10.6 mL, 145 mmol) was then added dropwise to the reaction mixture. After 20 min, the reaction was quenched with 500 mL of distilled water and the mixture was filtered. The yellow residue was then dried under IR lamp for at least 30 min. The crude product was directly used in the next step without further purification. Crude compound (20.0 g) was dissolved in methanol (260 mL), to which concentrated H₂SO₄ (21.9 mL, 388 mmol) was added. The mixture was heated under reflux for 48 hrs. The solvent was then removed in *vacuo* and the residue was dissolved in CH₂Cl₂ (200 mL), washed with water (2 x 100 mL), finally washed with aq NaHCO₃ (100 mL) and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave a yellow solid which was purified by flash column chromatography (silica gel) using hexane/ CH₂Cl₂ (4:1) as the eluent to give pure product **1r** as a bright yellow solid. Overall Yield: 14.3 g, 72%. ¹H NMR (300 MHz, CDCl₃) δ 11.99 (s, 1H), 8.15 (m, 2H), 7.01 (m, 1H), 4.02 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 169.16, 155.59, 137.97, 135.67, 131.30, 118.34, 115.78, 53.10. (Ref: Dumn, B.M.; Bruice, T. C. *J. Am. Chem. Soc.* **1970**, 92, 2410)

Compound 1s: **1r** (6.00 g, 30.4 mmol) was dissolved in DMF (125 mL) to which anhydrous K₂CO₃ (15.6 g, 113 mmol) and iodomethane (6.98 mL, 112 mmol) were added to it. The mixture was heated under reflux for 4 hrs. The reaction mixture was then filtered and the solvent was removed in *vacuo*. The residue was dissolved in CH₂Cl₂ (100 mL), washed with water (2 x 50 mL), and dried over anhydrous Na₂SO₄. Removal of CH₂Cl₂ gave a pure light yellow solid **1s**. Yield: 6.41 g, 82%. ¹H NMR (300 MHz, CDCl₃) δ 8.03 (m, 1H), 8.00 (m, 1H), 7.91 (d, 1H, *J* = 1.8), 3.99 (s, 3H), 3.94 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 164.42, 152.86, 145.17, 135.25, 128.02, 127.06, 123.50, 63.89, 52.39. HRMS-ESI: calculated for [M]⁺ (C₈H₇NO₅): *m/z* 211.0481 found: *m/z* 211.0480.

Compound 1t: **1s** (4.00 g, 19.0 mmol) was dissolved in hot methanol (10 mL) to which 1M NaOH (40 mL, 40.0 mmol) was added. The mixture was heated under reflux for 2 h and then quenched with water (100 mL). The aqueous layer was neutralized by addition of 1M HCl (80 mL) until the pH was at least 1. The precipitated crude product was collected by filtration, which was recrystallized from hot methanol to give a pure white solid **1t**. Yield: 3.45 g, 92%. ¹H NMR (300 MHz, CDCl₃) δ 8.28 (m, 1H), 8.03 (m, 1H), 7.36 (m, 1H), 4.08 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 164.97, 151.89, 144.49, 134.71, 127.31, 126.79, 122.79, 63.06. (Ref: Lloyd, H. A.; Warren, K. S.; Fales, H. M. *J. Am. Chem. Soc.* **1966**, 88, 5544)

Compound 2a: **1s** (3.16 g, 15.0 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 °C, using Pd/C (0.30 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure brown liquid. The resulting amine was immediately used for the next coupling. Acid **1t** (3.00 g, 15.2 mmol) was dissolved in CH₂Cl₂ (30 mL) to which 4-methylmorpholine (NMM (2.20 mL, 17.9 mmol) and ethyl chloroformate (1.96 mL, 16.4 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of above amine (2.70 g, 14.9 mmol) dissolved in CH₂Cl₂ (30 mL) was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (100 mL), followed by saturated NaHCO₃

(100 mL) and saturated NaCl (100 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2a** as a white solid. Yield: 3.49 g, 71%. ¹H NMR (300 MHz, CDCl₃) δ 10.37 (s, 1H), 8.80 (d, 1H, *J* = 8.2), 8.44 (d, 1H, *J* = 8.2), 7.99 (d, 1H, *J* = 7.9), 7.63 (d, 1H, *J* = 8.1), 7.41 (t, 1H, *J* = 8.1), 7.24 (t, 1H, *J* = 8.1), 4.10 (s, 3H), 3.95 (s, 6H). ¹³C NMR (125 MHz, CDCl₃) δ 165.85, 161.27, 151.46, 149.43, 136.47, 132.70, 128.75, 126.56, 124.60, 123.51, 64.47, 62.57. HRMS-ESI: calculated for [M+Na]⁺ (C₁₇H₁₆N₂O₇Na): *m/z* 383.0850 found: *m/z* 383.0856.

Compound 3a: 2a (3.46 g, 10.0 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 °C, using Pd-C (0.35 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1t** (2.06 g, 10.5 mmol) was dissolved in CH₂Cl₂ (50 mL) to which NMM (1.35 mL, 12.4 mmol) and ethyl chloroformate (1.08 mL, 11.3 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min after which a solution of the above amine (3.10 g, 9.04 mmol) dissolved in CH₂Cl₂ (50 mL) was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (100 mL), followed by saturated NaHCO₃ (100 mL) and saturated NaCl (100 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **3a** as a white solid. Yield: 3.64 g, 82%. ¹H NMR (300 MHz, CDCl₃) δ 10.25 (s, 1H), 10.23 (s, 1H), 8.85 (d, 1H, *J* = 7.9), 8.78 (d, 1H, *J* = 7.9), 8.47 (d, 1H, *J* = 7.9), 8.03 (d, 1H, *J* = 8.0), 7.91 (d, 1H, *J* = 7.9), 7.62 (d, 1H, *J* = 7.9), 7.40 (m, 2H), 7.22 (m, 1H), 4.14 (s, 3H), 3.98 (s, 3H), 3.96 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 162.81, 161.33, 151.34, 149.23, 147.29, 144.32, 136.59, 133.03, 131.97, 129.09, 128.97, 126.73, 126.63, 126.22, 125.79, 125.05, 124.71, 124.59, 124.42, 123.45, 64.45, 63.23, 62.50, 53.38, 52.30. HRMS-ESI: calculated for [M+Na]⁺ (C₂₅H₂₃N₃O₉): *m/z* 532.1327 found: *m/z* 532.1328.

Compound 4a: 3a (3.00 g, 6.09 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 °C, using Pd-C (0.60 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1t** (1.79 g, 9.10 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (50 mL) and DMF (0.42 mL) were added to the acid, followed by dropwise addition of oxalyl chloride, (COCl)₂, (1.05 mL, 7.27 mmol). The reaction mixture was allowed to stir for 2 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 15 mL dry CH₂Cl₂. The above amine (2.81 g, 6.06 mmol) was dissolved in 35 mL dry CH₂Cl₂ and triethylamine (TEA, 1.86 mL, 12.1 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 2 hrs and then was washed with aq NaHCO₃ (100 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **4a** as a white solid. Yield: 2.34 g, 61%. ¹H NMR (500 MHz, CDCl₃) δ 10.20 (s, 1H), 10.10 (s, 1H), 10.00 (s, 1H), 8.76 (m, 3H), 8.44 (m, 1H), 8.03 (m, 1H), 7.90 (m, 2H), 7.61 (m, 1H), 7.40 (m, 3H), 7.22 (m, 1H), 4.13 (s, 3H), 3.97 (s, 3H), 3.95 (s, 3H), 3.94 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.80, 162.86, 161.42, 151.21, 149.19, 147.17, 144.29, 136.39, 132.58, 131.86, 129.20, 128.57, 126.69, 126.57, 126.28, 126.14, 125.67, 124.63, 123.41, 64.40, 63.07, 62.37, 52.26. HRMS-ESI: calculated for [M+Na]⁺ (C₃₃H₃₀N₄O₁₁Na): *m/z* 681.1803 found: *m/z* 681.1791.

Compound 2h: 4a (0.61 g, 0.95 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 50 °C, using Pd-C (0.75 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1t** (0.27 g, 1.36 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (5 mL) and DMF (60 µL) were added to the acid, followed by dropwise addition of oxalyl chloride (142 µL, 1.12 mmol). The reaction mixture was allowed to stir for 2 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.57 g, 0.93 mmol) was dissolved in 25 mL dry CH₂Cl₂ and triethylamine, triethylamine (0.27 mL, 1.86 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 2 hrs and then was washed with aq NaHCO₃ (50 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using CH₂Cl₂/CH₃CN (10:1) as the eluent to give pure product **5a** as a white solid. Yield: 0.44 g, 61%. ¹H NMR (300 MHz, CDCl₃) δ 10.25 (d, 2H), 9.85 (s, 1H), 9.65 (s, 1H), 8.81 (m, 4H), 8.44 (m, 1H), 8.02 (m, 4H), 7.89 (m, 2H), 7.61 (m, 4H), 4.03 (s, 15H), 3.88 (m, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.56, 163.06, 162.81, 161.42, 151.25, 149.22, 147.24, 147.19, 144.14, 136.40, 132.17, 131.91, 128.84, 126.49, 125.69, 124.75, 123.25, 64.38, 63.14, 62.97, 52.10. HRMS-ESI: calculated for [M+Na]⁺ (C₄₁H₃₇N₃O₁₃Na): *m/z* 830.2280 found: *m/z* 830.2304.

Compound 2h: 2a (1.00 g, 2.78 mmol) was dissolved in hot methanol (20 mL) to which 1M KOH (10 mL, 10.0 mmol) and KCl (0.98 g, 10.0 mmol) was added. The mixture was heated under reflux for 2 h and then quenched with water (50 mL). The aqueous layer was neutralized by addition of 1M HCl (15 mL) until pH = 1. The precipitated crude product was collected by filtration, which was recrystallized from hot methanol to give a pure white solid **2g**. Yield: 0.80 g, 83%. ¹H NMR (300 MHz, CDCl₃) δ 10.39 (s, 1H), 8.93 (d, 1H, *J* = 8.2), 8.45 (d, 1H, *J* = 7.6), 8.00 (d, 1H, *J* = 7.6), 7.77 (d, 1H, *J* = 7.6), 7.43 (s, 1H), 7.31 (m, 1H), 4.10 (s, 3H), 4.03 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 167.32, 163.39, 150.76, 150.58, 144.40, 135.00, 132.52, 131.59, 127.79, 127.09, 126.37, 126.16, 125.14, 124.17. HRMS-ESI: calculated for [M+Na]⁺ (C₁₆H₁₄N₂O₇Na): *m/z* 345.0723 found: *m/z* 345.0714.

Compound 6a: 4a (0.36 g, 0.55 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 50 °C, using Pd-C (0.070 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **2h** (0.22 g, 0.66 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (5 mL) and DMF (40 µL) were added to the acid, followed by dropwise addition of oxalyl chloride (100 µL, 0.79 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.32 g, 0.51 mmol) was dissolved in 15 mL dry CH₂Cl₂ and triethylamine (0.15 mL, 1.02 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (30 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was purified by flash column chromatography (silica gel as the stationary phase) using CH₂Cl₂ / CH₃CN (10:1) as the eluent to give pure product **6a** as a white solid. Yield: 0.12 g, 19%. ¹H NMR (500 MHz, CDCl₃) δ 10.28 (s, 1H), 10.19 (s, 1H), 10.15 (s, 1H), 10.12 (s, 1H), 9.84 (s, 1H), 8.85 (m, 2H),

8.80 (m, 3H), 8.33 (d, 1H, $J = 7.8$) 7.82 (m, 5H), 7.51 (d, 1H, $J = 7.8$), 7.39 (m, 5H), 7.15 (d, 1H), 4.08 (s, 3H), 4.04 (s, 3H), 4.02 (s, 3H), 4.01 (s, 3H), 3.96 (s, 3H), 3.79 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3) δ 165.36, 163.34, 163.04, 162.93, 162.82, 161.32, 151.00, 149.09, 147.21, 147.19, 147.08, 144.10, 136.37, 133.12, 132.34, 132.16, 132.03, 129.06, 128.80, 126.79, 126.65, 126.55, 126.47, 126.36, 126.31, 126.18, 126.03, 125.97, 125.92, 125.84, 125.35, 125.13, 124.99, 124.88, 124.84, 124.68, 124.43, 123.10, 64.46, 63.26, 63.10, 63.00, 62.97, 62.25, 52.23. HRMS-ESI: calculated for $[\text{M}+\text{Na}]^+$ ($\text{C}_{49}\text{H}_{44}\text{N}_6\text{O}_{15}\text{Na}$): m/z 979.2957 found: m/z 979.2765.

Compound 2b: 1h (1.70 g, 8.00 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 $^\circ\text{C}$, using Pd/C (0.17 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure brown liquid. The resulting amine was immediately used for the next coupling. Acid **1t** (2.00 g, 10.1 mmol) was dissolved in CH_2Cl_2 (30 mL) to which NMM (2.00 mL, 18.3 mmol) and ethyl chloroformate (1.50 mL, 12.6 mmol) was added at 0 $^\circ\text{C}$. The reaction mixture was stirred for at least 15 min then a solution of above amine dissolved in CH_2Cl_2 (30 mL) was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO_4 (100 mL), followed by saturated NaHCO_3 (100 mL) and saturated NaCl (100 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2b** as a white solid. Yield: 2.40 g, 77%. ^1H NMR (500 MHz, CDCl_3) δ 10.35 (s, 1H), 8.47 (d, 1H, $J = 3.2$), 8.43 (d, 1H, $J = 8.1$), 7.98 (d, 1H, $J = 7.8$), 7.40 (t, 1H, $J = 8.1$), 7.13 (d, 1H, $J = 3.2$), 4.08 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 165.67, 161.29, 155.59, 151.48, 144.36, 143.30, 136.43, 133.40, 129.08, 128.80, 124.81, 123.76, 111.00, 110.73, 64.47, 62.57, 55.84, 52.39. HRMS-ESI: calculated for $[\text{M}]^+$ ($\text{C}_{18}\text{H}_{18}\text{N}_2\text{O}_8$): m/z 389.0990 found: m/z 389.0985.

Compound 2d: 1h (0.60 g, 2.49 mmol) was reduced by catalytic hydrogenation in THF (15 mL) at 40 $^\circ\text{C}$ for 3 h. The resulting amine was dissolved in CH_2Cl_2 (30 mL) was immediately used for the next coupling. Acid **1k** (0.74 g, 3.24 mmol) was dissolved in CH_2Cl_2 (30 mL) to which NMM (0.45 mL, 3.68 mmol) and ethyl chloroformate (0.40 mL, 3.34 mmol) was added at 0 $^\circ\text{C}$. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO_4 (30 mL), followed by saturated NaHCO_3 (30 mL) and saturated NaCl (30 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2d** as a yellow solid. Yield: 0.75 g, 72%. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 10.25 (s, 1H), 8.10 (d, 1H, $J = 3.3$), 7.70 (d, 1H, $J = 3.3$), 7.61 (d, 1H, $J = 3.5$), 7.04 (d, 1H, $J = 3.1$), 3.87 (m, 15H). δ 10.37 (s, 1H), 8.80 (d, 1H, $J = 6.57$), 8.44 (d, 1H, $J = 6.09$), 7.99 (d, 1H, $J = 6.24$), 7.63 (d, 1H, $J = 6.27$), 7.43 (m, 2H), 4.10 (s, 3H), 3.95 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3) δ 155.52, 144.72, 143.28, 133.37, 129.59, 123.74, 120.63, 111.64, 111.05, 110.62, 64.60, 62.65, 56.27, 55.81, 52.38. HRMS-ESI: calculated for $[\text{M}+\text{Na}]^+$ ($\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_9\text{Na}$): m/z 443.1061 found: m/z 443.1065.

Compound 2e: 1h (0.50 g, 2.37 mmol) was reduced by catalytic hydrogenation in THF (15 mL) at 60 $^\circ\text{C}$ for 3 h. The resulting amine was dissolved in CH_2Cl_2 (30 mL) was immediately used for the next coupling. Acid **1k** (0.90 g, 2.84 mmol) was dissolved in CH_2Cl_2 (30 mL) to which NMM (0.45 mL, 3.68 mmol) and ethyl

chloroformate (0.40 mL, 3.26 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (30 mL), followed by saturated NaHCO₃ (30 mL) and saturated NaCl (30 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2e** as a yellow solid. Yield: 0.90 g, 73%. ¹H NMR (300 MHz, DMSO-d₆) δ 10.49 (s, 1H), 8.48 (d, 1H, *J* = 3.2), 7.94 (d, 1H, *J* = 3.2), 7.49 (d, 1H, *J* = 3.2), 7.14 (d, 1H, *J* = 3.2), 4.03 (m, 2H), 4.02 (s, 3H), 3.94 (s, 3H), 3.89 (s, 3H), 3.86 (s, 3H), 1.81 (m, 2H), 1.35 (m, 10H), 0.92 (m, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.67, 161.27, 155.54, 155.18, 144.72, 144.64, 143.31, 133.43, 129.50, 123.78, 121.14, 115.09, 111.02, 110.64, 69.29, 64.59, 62.66, 55.81, 52.37, 31.75, 30.87, 29.21, 28.91, 25.85, 22.61, 14.05. HRMS-ESI: calculated for [M+Na]⁺ (C₂₆H₃₄N₂O₉Na): *m/z* 541.2157 found: *m/z* 541.2152.

Compound 3b: **2b** (1.05 g, 2.70 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 40 °C, using Pd-C (0.16 g, 15%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1t** (0.74 g, 3.30 mmol) was dissolved in CH₂Cl₂ (20 mL) to which NMM (0.50 mL, 4.06 mmol) and ethyl chloroformate (0.40 mL, 3.33 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min after which a solution of the above amine dissolved in CH₂Cl₂ (20 mL) was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (30 mL), followed by saturated NaHCO₃ (30 mL) and saturated NaCl (30 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **3b** as a white solid. Yield: 1.20 g, 78%. ¹H NMR (300 MHz, CDCl₃) δ 10.38 (s, 1H), 10.25 (s, 1H), 8.78 (d, 1H, *J* = 8.4), 8.54 (d, 1H, *J* = 2.8), 7.99 (d, 1H, *J* = 3.5), 7.91 (d, 1H, *J* = 8.0), 7.54 (d, 1H, *J* = 3.2), 7.37 (t, 1H, *J* = 7.9), 7.14 (d, 1H, *J* = 3.2), 4.07 (s, 3H), 3.97 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 161.16, 155.60, 147.29, 144.65, 133.66, 131.95, 129.52, 126.62, 125.71, 124.65, 123.64, 120.81, 114.63, 110.75, 110.41, 64.50, 63.19, 62.53, 56.27, 55.78, 52.32. HRMS-ESI: calculated for [M]⁺ (C₂₇H₂₇N₃O₁₁Na): *m/z* 592.1538 found: *m/z* 592.1534.

Compound 3c: **2d** (0.31 g, 0.74 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 °C, using Pd-C (0.040 g, 10%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1t** (0.22 g, 0.96 mmol) was dissolved in CH₂Cl₂ (10 mL) to which NMM (0.15 mL, 1.95 mmol) and ethyl chloroformate (0.12 mL, 1.43 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min after which a solution of the above amine dissolved in CH₂Cl₂ (10 mL) was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (20 mL), followed by saturated NaHCO₃ (20 mL) and saturated NaCl (20 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **3c** as a white solid. Yield: 0.37 g, 83%. ¹H NMR (300 MHz, CDCl₃) δ 10.39 (s, 2H), 8.54 (d, 1H, *J* = 3.2), 8.44 (d, 1H, *J* = 3.2), 7.98 (d, 1H, *J* = 3.2), 7.54 (d, 1H, *J* = 3.2), 7.44 (d, 1H, *J* = 3.2), 7.14 (d, 1H, *J* = 3.2), 4.06 (s, 3H), 3.95 (s, 3H), 3.92 (s, 9H), 3.90 (s, 3H), 3.86 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.73, 162.62, 161.18, 156.75, 155.67, 144.72, 143.07, 141.21, 133.75, 132.73, 129.53, 126.70, 125.02, 123.74, 122.06,

120.76, 120.19, 117.42, 114.81, 111.17, 110.91, 110.39, 64.57, 63.42, 62.58, 56.34, 55.88, 55.84, 52.39. HRMS-ESI: calculated for $[M+Na]^+$ ($C_{28}H_{29}N_3O_{12}Na$): m/z 622.1643 found: m/z 622.1646.

Compound 3d: **2e** (0.90 g, 1.84 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 60 °C for 3 h. The resulting amine was dissolved in CH_2Cl_2 (30 mL) was immediately used for the next coupling. Acid **1k** (0.60 g, 2.64 mmol) was dissolved in CH_2Cl_2 (30 mL) to which NMM (0.40 mL, 3.25 mmol) and ethyl chloroformate (0.35 mL, 2.92 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M $KHSO_4$ (30 mL), followed by saturated $NaHCO_3$ (30 mL) and saturated $NaCl$ (30 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **3d** as a yellow solid. Yield: 0.86 g, 67%. 1H NMR (300 MHz, $CDCl_3$) δ 10.39 (s, 1H), 10.37 (s, 1H), 8.54 (d, 1H, J = 3.2), 8.41 (d, 1H, J = 3.2), 7.98 (d, 1H, J = 3.2), 7.53 (d, 1H, J = 3.5), 7.42 (d, 1H, J = 3.2), 7.13 (d, 1H, J = 3.2), 4.06 (s, 3H), 4.03 (m, 2H), 3.95 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H), 3.86 (s, 3H), 1.78 (m, 2H), 1.31 (m, 10H), 0.85 (m, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 162.67, 161.13, 156.31, 155.71, 155.63, 144.68, 143.04, 141.02, 133.76, 132.60, 129.55, 126.59, 123.70, 120.75, 114.73, 111.69, 110.92, 110.84, 110.37, 68.69, 64.53, 63.38, 62.55, 56.30, 55.81, 52.36, 31.78, 29.28, 29.20, 29.14, 15.95, 22.62, 14.06. HRMS-ESI: calculated for $[M]^+$ ($C_{35}H_{43}N_3O_{12}$): m/z 720.2739 found: m/z 720.2757.

Compound 1u: **1k** (0.40 g, 1.76 mmol), isopropamine (0.14 g, 2.37 mmol) was dissolved in CH_2Cl_2 (30 mL), to which EDC (0.50 g, 2.60 mmol) and HOBT (0.50 g, 3.70 mmol) was added. The reaction mixture was stirred for overnight at room temperature. The reaction mixture was washed with 1M $KHSO_4$ (30 mL), followed by saturated $NaHCO_3$ (30 mL) and saturated $NaCl$ (30 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the product **1u**. Yield: 0.45 g, 95%. 1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, 1H, J = 3.2), 7.41 (d, 1H, J = 3.2), 7.30 (s, 1H), 3.90 (s, 1H), 3.87 (s, 1H), 1.28 (s, 3H), 1.27 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.01, 156.24, 145.04, 143.44, 131.38, 121.15, 114.16, 64.59, 57.59, 56.90, 46.15, 45.53, 42.55. HRMS-EI: calculated for $[M]^+$ ($C_8H_8O_4$): m/z 268.1059 found: m/z 268.1055.

Compound 2f: **1u** (0.45 g, 1.68 mmol) was reduced by catalytic hydrogenation in THF (30 mL) at 40 °C for 3 h. The resulting amine was dissolved in CH_2Cl_2 (40 mL) was immediately used for the next coupling. Acid **1l** (0.74 g, 2.24 mmol) was dissolved in CH_2Cl_2 (40 mL) to which NMM (0.40 mL, 3.27 mmol) and ethyl chloroformate (0.30 mL, 2.45 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M $KHSO_4$ (30 mL), followed by saturated $NaHCO_3$ (30 mL) and saturated $NaCl$ (30 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2f** as a yellow solid. Yield: 0.35g, 64%. 1H NMR (300 MHz, $CDCl_3$) δ 10.24 (s, 1H), 8.34 (d, 1H, J = 3.2), 7.92 (d, 1H, J = 3.2), 7.50 (d, 1H, J = 3.9), 7.26 (d, 1H, J = 3.2), 7.22 (d, 1H, J = 3.2), 4.33 (m, 1H), 4.03 (s, 5H), 3.82 (s, 6H), 1.80 (m, 2H), 1.24 (m, 16H), 0.88 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.44, 161.88, 157.14, 155.99, 145.33, 145.13, 141.52, 133.07, 130.33, 128.14, 121.89, 115.76, 110.88, 110.66, 69.99, 65.33, 63.24, 56.48,

42.24, 32.43, 29.89, 29.85, 29.59, 26.53, 23.29, 14.74. HRMS-ESI: calculated for $[M]^-$ ($C_{28}H_{39}N_3O_8$): m/z 544.2664 found: m/z 544.2680.

Compound 2c: **1s** (1.60 g, 8.80 mmol) was reduced by catalytic hydrogenation in THF (50 mL) at 40 °C, using Pd-C (0.16 g, 10%) as the catalyst for 3 h. The resulting amine was dissolved in CH_2Cl_2 (60 mL) was immediately used for the next coupling. Acid **1l** (3.44 g, 10.6 mmol) was dissolved in CH_2Cl_2 (90 mL) to which NMM (1.40 mL, 11.2 mmol) and ethyl chloroformate (1.50 mL, 12.2 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then the solution of above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M $KHSO_4$ (100 mL), followed by saturated $NaHCO_3$ (100 mL) and saturated NaCl (100 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was purified by flash column chromatography (silica gel) using hexane/ethyl acetate (8:1 v/v) as the eluent to give pure yellow solid **2c**. Yield: 2.00 g, 47%. 1H NMR (300 MHz, $CDCl_3$) δ 10.46 (s, 1H), 8.77 (d, 1H, $J = 5.1$), 7.93 (d, 1H, $J = 3.5$), 7.61 (d, 1H, $J = 8.9$), 7.48 (d, 1H, $J = 3.5$), 7.21 (m, 1H), 4.02 (m, 2H), 3.94 (s, 6H), 1.81 (m, 2H), 1.44 (m, 2H), 1.30 (m, 8H), 0.84 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.84, 161.22, 155.17, 149.45, 144.70, 144.61, 132.74, 129.60, 126.50, 124.55, 124.23, 123.52, 121.27, 114.94, 69.26, 64.56, 62.55, 52.31, 31.74, 29.20, 29.15, 28.91, 25.85, 22.60, 14.04. HRMS-ESI: calculated for $[M+Na]^+$ ($C_{25}H_{32}N_2O_8Na$): m/z 511.2051 found: m/z 511.2038

Compound 3e: **2c** (1.00 g, 2.18 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 40 °C, using Pd-C (0.10 g, 10%) as the catalyst for 3 h. The resulting amine was dissolved in CH_2Cl_2 (20 mL) was immediately used for the next coupling. Acid **1m** (0.70 g, 2.75 mmol) was dissolved in CH_2Cl_2 (30 mL) to which NMM (0.40 mL, 3.25 mmol) and ethyl chloroformate (0.35 mL, 2.93 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then the solution of above amine was added. The reaction mixture was allowed to stir continuously overnight at 50 °C. The reaction mixture was washed with 1M $KHSO_4$ (50 mL), followed by saturated $NaHCO_3$ (50 mL) and saturated NaCl (50 mL). Drying over Na_2SO_4 and removal of solvent in *vacuo* gave the crude product, which was purified by flash column chromatography (silica gel) using hexane/ethyl acetate (5:1 v/v) as the eluent to give pure yellow solid **3e**. Yield: 1.00 g, 52%. 1H NMR (300 MHz, $CDCl_3$) δ 10.37 (s, 1H), 10.36 (s, 1H), 8.84 (d, 1H, $J = 3.2$), 8.42 (d, 1H, $J = 3.3$), 7.94 (d, 1H, $J = 3.2$), 7.60 (d, 1H, $J = 1.7$), 7.50 (d, 1H, $J = 3.2$), 7.42 (d, 1H, $J = 3.2$), 7.24 (m, 1H), 4.65 (m, 1H), 4.06 (s, 3H), 4.05 (m, 2H), 3.96 (s, 3H), 3.95 (s, 3H), 3.91 (s, 3H), 1.83 (m, 2H), 1.54 (s, 6H), 1.40 (m, 8H), 1.24 (m, 2H), 0.88 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.89, 162.64, 161.24, 156.31, 154.17, 149.22, 144.77, 144.33, 141.00, 133.08, 132.62, 129.51, 126.71, 126.10, 124.52, 124.33, 123.50, 122.25, 116.26, 111.58, 111.04, 71.56, 68.65, 64.47, 63.33, 62.43, 52.27, 31.77, 29.27, 29.16, 25.95, 22.61, 21.73, 14.03. HRMS-ESI: calculated for $[M]^+$ ($C_{36}H_{45}N_3O_{11}$): m/z 718.2946 found: m/z 718.2952.

Compound 4b: **3e** (0.84 g, 1.20 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 40 °C, using Pd-C (0.17 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1q** (0.30 g, 1.42 mmol) was placed in a very dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH_2Cl_2 (8 mL) and DMF (64 μ L) were added to the acid, followed by dropwise addition of oxalyl

chloride (0.16 mL, 1.26 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.80 g, 1.20 mmol) was dissolved in 15 mL dry CH₂Cl₂ and triethylamine (0.60 mL, 4.2 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (50 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using hexane/ethyl acetate (2:1 v/v) as the eluent to give pure **4b** as white solid. Yield: 0.59 g, 57%. ¹H NMR (300 MHz, CDCl₃) δ 10.33 (s, 1H), 10.14 (s, 1H), 10.10 (s, 1H), 8.84 (d, 1H, *J* = 7.0), 8.46 (d, 1H, *J* = 2.8), 8.41 (d, 1H, *J* = 3.2), 8.23 (d, 1H, *J* = 1.7), 7.83 (d, 1H, *J* = 1.7), 7.61 (d, 1H, *J* = 7.0), 7.42 (m, 2H), 7.23 (m, 1H), 4.66 (m, 1H), 4.09 (s, 3H), 4.05 (m, 2H), 3.96 (s, 3H), 3.94 (s, 6H), 3.91 (s, 3H), 2.48 (s, 3H), 1.84 (m, 2H), 1.48 (s, 6H), 1.39 (m, 8H), 1.22 (m, 2H), 0.87 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.92, 162.79, 162.74, 161.64, 156.33, 155.17, 149.26, 149.03, 143.98, 140.85, 136.83, 135.67, 133.08, 132.93, 132.66, 129.13, 128.63, 126.74, 126.60, 126.18, 126.04, 124.68, 124.40, 123.44, 113.06, 112.39, 111.42, 111.08, 110.80, 70.74, 68.62, 64.40, 63.31, 63.24, 62.42, 52.37, 31.80, 29.66, 29.30, 29.22, 29.17, 25.97, 22.64, 21.97, 20.68, 14.09. HRMS-ESI: calculated for [M+Na]⁺ (C₄₅H₅₄N₄O₁₃Na): *m/z* 881.3580 found: *m/z* 881.3572.

Compound 5b: 4b (0.40 g, 0.47 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 50 °C, using Pd-C (0.08 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1m** (0.24 g, 0.94 mmol) was placed in a very dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (8 mL) and DMF (40 μL) were added to the acid, followed by dropwise addition of oxalyl chloride (0.10 mL, 0.78 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.39 g, 0.47 mmol) was dissolved in 10 mL dry CH₂Cl₂ and triethylamine (0.40 mL, 2.8 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (50 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using hexane/ethyl acetate (2:1 v/v) as the eluent to give pure **5b** as yellow solid. Yield: 0.23 g, 46%. ¹H NMR (300 MHz, CDCl₃) δ 10.35 (s, 1H), 10.22 (s, 1H), 10.10 (s, 1H), 9.86 (s, 1H), 8.82 (d, 1H, *J* = 8.2), 8.61 (d, 1H, *J* = 1.7), 8.43 (m, 2H), 7.91 (d, 1H, *J* = 3.3), 7.68 (d, 1H, *J* = 4.7), 7.59 (d, 1H, *J* = 1.7), 7.47 (d, 1H, *J* = 3.3), 7.39 (m, 2H), 7.20 (m, 1H), 4.64 (m, 1H), 4.05 (s, 3H), 4.04 (m, 2H), 3.97 (s, 3H), 3.94 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 2.45 (s, 3H), 1.79 (m, 2H), 1.47 (s, 6H), 1.37 (m, 2H), 1.28 (m, 8H), 0.86 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.61, 163.24, 162.89, 162.75, 161.41, 156.32, 155.18, 154.18, 149.32, 145.14, 144.67, 144.32, 140.98, 140.80, 135.88, 133.12, 132.94, 131.61, 129.76, 126.83, 126.78, 126.61, 126.24, 126.10, 125.40, 124.72, 124.38, 123.33, 122.27, 119.88, 116.22, 113.02, 112.27, 111.89, 111.61, 110.91, 71.56, 70.74, 68.64, 64.45, 63.14, 62.27, 31.76, 29.62, 29.27, 29.17, 25.95, 22.60, 21.98, 21.70, 21.30, 14.01. HRMS-ESI: calculated for [M+Na]⁺ (C₅₆H₆₇N₅O₁₆Na): *m/z* 1088.4755 found: *m/z* 1088.4750.

Compound 5c: 4b (0.20 g, 0.24 mmol) was reduced by catalytic hydrogenation in THF (10 mL) at 50 °C, using Pd-C (0.040 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1q** (0.10 g, 0.47 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (5 mL) and DMF (20 µL) were added to the acid, followed by dropwise addition of oxalyl chloride (0.060 mL, 0.50 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.19 g, 0.24 mmol) was dissolved in 5 mL dry CH₂Cl₂ and triethylamine (0.20 mL, 1.40 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (20 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using hexane/ethyl acetate (2:1 v/v) as the eluent to give pure **5c** as yellow solid. Yield: 0.12 g, 49%. ¹H NMR (500 MHz, CDCl₃) δ 10.28 (s, 1H), 10.21 (s, 1H), 9.95 (s, 1H), 9.84 (s, 1H), 8.83 (d, 1H, *J* = 8.2), 8.79 (m, 3H), 7.92 (d, 1H, *J* = 3.1), 7.90 (m, 3H), 7.61 (d, 1H, *J* = 7.9), 7.49 (d, 1H, *J* = 3.1), 7.40 (m, 3H), 7.20 (m, 1H), 4.65 (m, 1H), 4.06 (s, 3H), 4.02 (s, 6H), 3.96 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 1.38 (s, 6H). ¹H NMR (500 MHz, CDCl₃) δ 10.35 (s, 1H), 10.10 (s, 2H), 9.85 (s, 1H), 8.83 (d, 1H, *J* = 8.2), 8.60 (d, 1H, *J* = 1.7), 8.43 (m, 2H), 8.22 (d, 1H, *J* = 3.3), 7.79 (d, 1H, *J* = 4.7), 7.68 (d, 1H, *J* = 1.7), 7.60 (d, 1H, *J* = 3.3), 7.39 (m, 2H), 7.21 (m, 1H), 4.65 (m, 1H), 4.08 (s, 3H), 4.04 (m, 2H), 3.97 (s, 3H), 3.95 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 2.46 (s, 3H), 2.44 (s, 3H), 1.79 (m, 2H), 1.47 (s, 6H), 1.37 (m, 2H), 1.28 (m, 8H), 0.87 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.60, 163.26, 162.88, 162.74, 161.65, 156.28, 155.12, 149.29, 149.05, 145.10, 143.82, 140.94, 140.78, 136.78, 135.87, 135.52, 133.09, 132.90, 131.58, 129.24, 129.03, 128.91, 128.81, 128.69, 128.51, 128.34, 126.81, 126.69, 126.51, 128.33, 126.81, 126.70, 126.52, 126.12, 125.45, 124.72, 124.40, 123.25, 113.00, 112.20, 111.57, 110.83, 70.69, 68.59, 64.33, 63.16, 62.29, 52.11, 31.76, 29.62, 29.27, 29.18, 25.94, 22.60, 21.96, 21.33, 20.64, 14.04. HRMS-ESI: calculated for [M]⁺ (C₅₄H₆₂N₅O₁₅): *m/z* 1020.4242 found: *m/z* 1020.4203.

Compound 2g: 1t (4.00 g, 18.9 mmol) was reduced by catalytic hydrogenation in THF (100 mL) at 50 °C for 3 h. The resulting amine was dissolved in CH₂Cl₂ (100 mL) was immediately used for the next coupling. Acid **1m** (6.00 g, 23.5 mmol) was dissolved in CH₂Cl₂ (150 mL) to which NMM (3.60 mL, 28.6 mmol) and ethyl chloroformate (3.20 mL, 26.0 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at room temperature. The reaction mixture was washed with 1M KHSO₄ (200 mL), followed by saturated NaHCO₃ (200 mL) and saturated NaCl (200 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **2g**. Yield: 4.91 g, 62%. ¹H NMR (300 MHz, CDCl₃) δ 10.48 (s, 1H), 8.79 (d, 1H, *J* = 8.2), 7.93 (d, 1H, *J* = 3.2), 7.62 (d, 1H, *J* = 7.8), 7.47 (d, 1H, *J* = 3.2), 7.24 (m, 1H), 4.65 (m, 1H), 4.60 (s, 3H), 4.02 (s, 3H), 3.94 (s, 3H), 1.37 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 165.80, 161.20, 153.98, 149.41, 144.47, 132.73, 129.59, 126.46, 124.51, 124.20, 123.50, 122.30, 116.13, 71.46, 64.51, 62.51, 52.28, 21.71. HRMS-ESI: calculated for [M+Na]⁺ (C₂₀H₂₂N₂O₈Na): *m/z* 440.1190 found: *m/z* 440.1194.

Compound 3f: **2g** (2.70 g, 6.45 mmol) was reduced by catalytic hydrogenation in THF (80 mL) at 50 °C for 3 h. The resulting amine dissolved in CH₂Cl₂ (80 mL) was immediately used for the next coupling. Acid **11** (2.50 g, 7.69 mmol) was dissolved in CH₂Cl₂ (70 mL) to which NMM (1.24 mL, 10.1 mmol) and ethyl chloroformate (1.00 mL, 8.45 mmol) was added at 0 °C. The reaction mixture was stirred for at least 15 min then a solution of the above amine was added. The reaction mixture was allowed to stir continuously overnight at 50 °C. The reaction mixture was washed with 1M KHSO₄ (60 mL), followed by saturated NaHCO₃ (60 mL) and saturated NaCl (60 mL). Drying over Na₂SO₄ and removal of solvent in *vacuo* gave the crude product, which was recrystallized from methanol to give the pure product **3f**. Yield: 3.70 g, 83%. ¹H NMR (300 MHz, CDCl₃) δ 10.65 (s, 1H), 10.42 (s, 1H), 8.84 (d, 1H, *J* = 3.2), 8.50 (d, 1H, *J* = 3.2), 8.01 (d, 1H, *J* = 3.2), 7.61 (d, 1H, *J* = 8.0), 7.39 (d, 1H, *J* = 3.2), 7.23 (m, 1H), 7.11 (d, 1H, *J* = 2.9), 7.24 (m, 1H), 4.65 (m, 1H), 4.06 (s, 3H), 4.61 (m, 2H), 4.04 (m, 2H), 3.94 (s, 6H), 3.91 (s, 3H), 3.89 (s, 3H), 1.85 (m, 2H), 1.56 (s, 6H), 1.43 (m, 8H), 1.27 (m, 2H), 0.85 (m, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 165.91, 162.64, 161.24, 155.29, 155.02, 149.21, 144.62, 144.45, 140.93, 133.05, 132.64, 129.44, 126.70, 126.13, 124.52, 124.35, 123.43, 121.25, 115.12, 112.28, 112.53, 70.72, 69.29, 64.52, 63.33, 62.45, 52.32, 50.77, 31.73, 29.64, 29.18, 29.14, 28.87, 25.83, 22.59, 21.95, 14.08. HRMS-ESI: calculated for [M+Na]⁺ (C₃₆H₄₅N₃O₁₁Na): *m/z* 719.2846 found: *m/z* 719.2980.

Compound 3g: **3f** (0.38 g, 0.54 mmol) was dissolved in hot methanol (10 mL) to which 1M KOH (1.37 mL, 1.37 mmol) and KCl (0.14 g, 1.82 mmol) was added. The mixture was heated under reflux for 2 h and then quenched with water (20 mL). The aqueous layer was neutralized by addition of 1M HCl (2.0 mL) until the pH was at least 1. The precipitated crude product was collected by filtration, which was recrystallized from hot methanol to give a pure white solid **3g**. Yield: 0.34 g, 93%. ¹H NMR (500 MHz, CDCl₃) δ 10.45 (s, 3H), 10.30 (s, 3H), 8.55 (d, 1H, *J* = 7.6), 7.96 (d, 1H, *J* = 3.2), 7.65 (d, 1H, *J* = 3.2), 7.57 (d, 1H, *J* = 3.2), 7.50 (d, 1H, *J* = 7.6), 7.25 (d, 1H, *J* = 3.2), 7.22 (m, 1H), 4.61 (m, 1H), 4.08 (s, 3H), 4.07 (m, 2H), 4.01 (s, 3H), 3.85 (s, 6H), 4.03 (s, 3H), 1.73 (s, 6H), 1.41 (m, 2H), 1.31 (m, 8H), 1.28 (m, 2H), 0.84 (m, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 166.81, 162.94, 162.52, 154.26, 153.47, 149.22, 144.48, 143.27, 142.76, 132.52, 132.31, 127.38, 125.87, 125.23, 124.32, 123.80, 120.1, 114.36, 112.32, 112.08, 70.15, 68.85, 64.07, 62.86, 62.23, 31.25, 28.67, 28.39, 25.47, 22.10, 21.75, 13.95. HRMS-ESI: calculated for [M+Na]⁺ (C₃₅H₄₃N₃O₁₁Na): *m/z* 704.2790 found: *m/z* 704.2801.

Compound 6b: Compound **3a** (0.20 g, 0.39 mmol) was reduced by catalytic hydrogenation in THF (15 mL) at 50 °C, using Pd-C (0.040 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **3g** (0.30 g, 0.44 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (5 mL) and DMF (27 μL) were added to the acid, followed by dropwise addition of oxalyl chloride (67 μL, 0.53 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.17 g, 0.36 mmol) was dissolved in 10 mL dry CH₂Cl₂ and triethylamine (0.10 mL, 0.69 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (50 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography

(silica gel as the stationary phase) using CH₂Cl₂/CH₃CN (20:1 v/v) as the eluent to give pure product **6b** as a white solid. Yield: 25 mg, 6%. ¹H NMR (500 MHz, CDCl₃) δ 10.20 (s, 2H), 10.12 (s, 1H), 10.09 (s, 1H), 10.08 (s, 1H), 9.82 (s, 1H), 8.65 (m, 2H), 8.61 (m, 2H), 8.26 (d, 1H, *J* = 3.2), 7.74 (m, 2H), 7.68 (d, 1H, *J* = 7.8), 7.62 (d, 1H, *J* = 3.2), 7.31 (d, 1H, *J* = 7.8), 7.21 (m, 3H), 7.16 (d, 1H, *J* = 3.2), 6.95 (t, 1H), 4.49 (m, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.78 (s, 3H), 3.63 (s, 3H), 3.61 (s, 3H), 1.66 (m, 2H), 1.46 (s, 6H), 1.29 (m, 8H), 1.13 (m, 2H), 0.63 (m, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 165.22, 163.26, 162.83, 162.74, 161.11, 155.22, 155.14, 149.00, 147.26, 147.18, 147.02, 144.32, 144.04, 140.80, 133.09, 132.77, 132.41, 132.16, 129.32, 126.68, 126.58, 126.48, 126.38, 126.28, 126.06, 125.90, 125.86, 125.76, 125.26, 124.87, 124.78, 124.58, 124.25, 122.99, 121.34, 114.71, 112.83, 112.51, 70.73, 69.19, 64.45, 63.34, 63.00, 62.91, 62.13, 53.14, 50.70, 31.70, 29.61, 29.17, 29.11, 28.87, 25.84, 22.56, 21.91, 14.00. HRMS-ESI: calculated for [M+Na]⁺ (C₄₁H₃₇N₃O₁₃Na): *m/z* 1165.4377 found: *m/z* 1165.4356.

Compound 5d: 4a (0.50 g, 0.734 mmol) was reduced by catalytic hydrogenation in THF (20 mL) at 50 °C, using Pd-C (0.14 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1m** (0.40 g, 1.56 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (10 mL) and DMF (0.10 mL) were added to the acid, followed by dropwise addition of oxalyl chloride (0.20 mL, 1.60 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.48 g, 0.73 mmol) was dissolved in 10 mL dry CH₂Cl₂ and triethylamine (0.30 mL, 2.10 mmol) before addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (40 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using hexane/ethyl acetate (2:1 v/v) as the eluent to give pure **5d** as yellow solid. Yield: 0.33 g, 52%. ¹H NMR (500 MHz, CDCl₃) δ 10.28 (s, 1H), 10.21 (s, 1H), 9.95 (s, 1H), 9.84 (s, 1H), 8.83 (d, 1H, *J* = 8.2), 8.79 (m, 3H), 7.92 (d, 1H, *J* = 3.1), 7.90 (m, 3H), 7.61 (d, 1H, *J* = 7.9), 7.49 (d, 1H, *J* = 3.1), 7.40 (m, 3H), 7.20 (m, 1H), 4.65 (m, 1H), 4.06 (s, 3H), 4.02 (s, 6H), 3.96 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H), 1.38 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 165.64, 163.17, 163.08, 162.88, 161.45, 154.19, 149.27, 147.29, 147.20, 144.65, 144.28, 133.04, 132.20, 132.02, 126.82, 126.66, 126.52, 126.39, 126.17, 125.87, 125.73, 125.09, 124.93, 124.84, 124.73, 124.44, 123.29, 122.36, 116.23, 71.54, 64.54, 63.21, 63.03, 62.36, 52.16, 29.65, 21.71. HRMS-ESI: calculated for [M+Na]⁺ (C₄₄H₄₃N₅O₁₄Na): *m/z* 888.2699 found: *m/z* 888.2723.

Compound 6c: 5d (0.10 g, 0.12 mmol) was reduced by catalytic hydrogenation in THF (5 mL) at 40 °C, using Pd-C (0.020 g, 20%) as the catalyst for 3 h. The reaction mixture was then filtered and the solvent removed in *vacuo* to give the pure amine which was immediately used for the next coupling. Acid **1q** (0.15 g, 0.71 mmol) was placed in a *very* dry round bottom flask and saturated with nitrogen gas. Freshly-prepared dry CH₂Cl₂ (4 mL) and DMF (32 μL) were added to the acid, followed by dropwise addition of oxalyl chloride (0.080 mL, 0.63 mmol). The reaction mixture was allowed to stir for 4 hrs. The solvent was then removed in *vacuo* and saturated with nitrogen gas before addition of 10 mL dry CH₂Cl₂. The above amine (0.090 g, 0.12 mmol) was dissolved in 5 mL dry CH₂Cl₂ and triethylamine (0.060 mL, 0.42 mmol) before

addition to the reaction mixture above. The reaction mixture was stirred at 50 °C for 6 hrs and then was washed with aq NaHCO₃ (10 mL). Drying over anhydrous Na₂SO₄ and removal of solvent in *vacuo* gave the crude product which was recrystallised from methanol and further purified by flash column chromatography (silica gel as the stationary phase) using hexane/ethyl acetate (1.5:1 v/v) as the eluent to give pure **6c** as white solid. Yield: 38 mg, 31%. ¹H NMR (300 MHz, CDCl₃) δ 10.28 (s, 1H), 10.25 (s, 1H), 10.15 (s, 1H), 10.14 (s, 1H), 9.85 (s, 1H), 8.83 (m, 2H), 8.81 (m, 2H), 8.46 (d, 1H, *J* = 3.2), 8.15 (d, 1H, *J* = 1.9), 7.94 (m, 3H), 7.68 (d, 1H, *J* = 1.9), 7.54 (d, 1H, *J* = 1.9), 7.52 (d, 1H, *J* = 1.9), 7.45 (m, 3H), 7.18 (m, 1H), 4.71 (m, 1H), 4.15 (s, 3H), 4.14 (s, 3H), 4.07 (s, 3H), 4.06 (s, 3H), 4.05 (s, 3H), 4.00 (s, 3H), 3.82 (s, 3H), 2.06 (s, 3H), 1.42 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 165.26, 163.29, 162.87, 162.79, 161.40, 155.17, 149.04, 148.73, 147.19, 147.04, 143.69, 140.77, 136.74, 135.61, 133.13, 132.80, 132.42, 132.33, 132.16, 129.01, 128.36, 126.72, 126.62, 126.51, 126.43, 126.31, 126.07, 125.92, 125.81, 125.30, 124.89, 124.82, 124.61, 124.24, 123.06, 112.85, 112.44, 70.72, 64.33, 63.36, 63.04, 62.94, 62.19, 60.33, 52.18, 29.64, 21.94, 20.98, 20.64, 14.14. HRMS-ESI: calculated for [M]⁺ (C₅₃H₅₁N₆O₁₆): *m/z* 1027.3366 found: *m/z* 1027.3362.

Amide Hydrogen-Deuterium Exchange Experiments: Solutions of oligomers (5 mM) were prepared by dissolving the compounds in 50% DMSO-*d*₆ in CDCl₃ (total volume: 0.95 mL) and the spectra were recorded at room temperature as the reference spectra at *t* = 0. The H-D exchange experiment was initiated by adding 0.05 mL of D₂O into the samples, which resulted in a solution in a mixed solvent of D₂O/DMSO-*d*₆/CDCl₃ (2:19:19 v/v). The resultant spectra were then recorded (500 MHz) at appropriate time intervals, based on which the time dependent peak areas of the amide protons were obtained and fitted into the pseudo-first-order reaction rate equation of $(I_t - I)/(I_0 - I_\infty) = e^{-kt}$, where *I_t*, *I*, and *I₀*, correspond to the integrated area of the corresponding proton at *t* = *t*, *t* = ∞, *t* = 0; *k* is the decayrate constant. The half-life *T*_{1/2} is related to *k* by *T*_{1/2} = ln2/*k*. Thus, the half-life *T*_{1/2} was obtained by fitting the time-dependent peak areas into the above equation $[(I_t - I_\infty)/(I_0 - I_\infty) = e^{-kt}]$ with Origin 7.7 program.

Table S1. Chemical shifts (ppm)^a and the half-lives (hrs, in parenthesis) of H-D exchange^b of amide protons.

oligomer	H ₆	H ₁₁	H ₁₆	H ₂₁	H ₂₆
2a	10.36 (0.13)				
2b	10.37 (0.20)				
2c	10.47 (0.90)				
2d	10.25 (0.24)				
2e	10.49 (0.56)				
2f	10.24 (0.30)	8.70 (0.21)			
2g	10.49 (0.83)				
3a	10.21 (0.04)	10.23 (0.27)			
3b	10.24 (0.05)	10.37 (0.24)			
3c	10.35 (0.08)	10.38 (1.34)			
3d	10.36 (0.11)	10.38 (0.65)			
3e	10.35 (0.07)	10.36 (0.90)			
3f	10.33 (0.05)	10.35 (0.72)			
4a	10.20 (0.63)	10.10 (0.03)	10.00 (0.06)		
4b	10.33 (0.92)	10.14 (0.11)	10.10 (0.08)		
5a	10.25 (0.33)	9.85 (0.05)	9.85 (0.20)	10.25 (0.27)	
5b	10.35 (1.90)	9.85 (0.07)	9.65 (0.28)	10.25 (0.37)	
5c	10.35 (1.25)	10.10 (0.08)	9.85 (0.24)	10.10 (0.32)	
5d	10.28 (0.14)	10.21 (0.09)	9.95 (0.09)	9.84 (0.21)	
6a	10.19 (0.07)	10.12 (0.09)	9.84 (0.06)	10.28 (0.11)	10.15 (0.38)
6b	10.12 (0.42)	10.08 (0.29)	9.81 (0.27)	10.21 (0.40)	10.09 (5.79)
6c	10.28 (0.21)	10.25 (0.17)	10.15 (0.21)	10.15 (0.40)	9.85 (1.20)

^a Chemical shifts were measured at 1 mM in CDCl₃ (500MHz) at room temperature. ^b Half-lives of H-D exchange data in parenthesis were measured at 5 mM in 5% D₂O/47.5% DMSO-*d*₆ (v:v) in CDCl₃ at room temperature.

d)

Ab Initio Molecular Modelling: All the calculations were carried out by utilizing the Gaussian03 program package.¹ The geometry optimizations were performed at the density functional theory (DFT) level, and the Becke's three parameter hybrid functional with the Lee-Yang-Parr correlation functional (B3LYP)² method was employed to do the calculations. The 6-31G*^{3,4} basis from the Gaussian basis set library has been used in all the calculations. All the trimers and hexamers were relaxed fully without any symmetry constraints. The harmonic vibrational frequencies and zero-point energy corrections were calculated at the same level of theory. Single point energy were obtained at the B3LYP level in conjunction with the 6-311+G(2d,p) basis set with use of the above optimized geometries, i.e., B3LYP/6-311+G(2d,p)//B3LYP/6-31G(d).

Determination of Crystal Structures: Data were collected on a Bruker APEX diffractometer with a CCD detector and graphite-monochromated MoK α radiation using a sealed tube (2.4 kW) at 223(2) K. Absorption corrections were made with the program SADABS⁵ and the crystallographic package SHELXTL⁶ was used for all calculations. In the final least-squares refinement cycles on $|F|^2$, the model converged at $R1 = 0.1335$, $wR2 = 0.1924$, $GoF = 1.081$ for 6245 ($I \geq 2\sigma(I)$) reflections.

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3. Petersson, G. A.; Bennett, A.; Tensfeldt, T. G.; Al-Laham, M. A.; Shirley, W. A.; Mantzaris, J. *J. Chem. Phys.* 1988, 89, 2193.
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5. Sheldrick, G. M.; *SADABS Software for Empirical Absorption Corrections, University of Göttingen (Germany), 2000.*
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X-Ray Crystal Data

Crystal data and structure refinement for **1c**

Identification code	7098	
Empirical formula	C ₁₆ H ₂₄ O ₄	
Formula weight	280.35	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.6816(6) Å	α = 84.4210(10)°.
	b = 11.8460(7) Å	β = 75.4620(10)°.
	c = 14.8820(9) Å	γ = 68.0090(10)°.
Volume	1531.93(16) Å ³	
Z	4	
Density (calculated)	1.216 Mg/m ³	
Absorption coefficient	0.086 mm ⁻¹	
F(000)	608	
Crystal size	0.60 x 0.50 x 0.14 mm ³	
Theta range for data collection	1.41 to 27.50°.	
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 15, -19 ≤ l ≤ 19	
Reflections collected	19300	
Independent reflections	7021 [R(int) = 0.0305]	
Completeness to theta = 27.50°	99.7 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9881 and 0.9503	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	7021 / 0 / 367	
Goodness-of-fit on F ²	1.031	
Final R indices [I > 2σ(I)]	R1 = 0.0552, wR2 = 0.1398	
R indices (all data)	R1 = 0.0690, wR2 = 0.1486	
Largest diff. peak and hole	0.349 and -0.220 e.Å ⁻³	

Crystal data and structure refinement for **2a**

Identification code	8008	
Empirical formula	C17 H16 N2 O7	
Formula weight	360.32	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 6.9923(4) Å	$\alpha = 90^\circ$.
	b = 28.3844(18) Å	$\beta = 91.323(2)^\circ$.
	c = 8.1995(5) Å	$\gamma = 90^\circ$.
Volume	1626.94(17) Å ³	
Z	4	
Density (calculated)	1.471 Mg/m ³	
Absorption coefficient	0.116 mm ⁻¹	
F(000)	752	
Crystal size	0.60 x 0.30 x 0.16 mm ³	
Theta range for data collection	1.43 to 27.43°.	
Index ranges	-8 ≤ h ≤ 9, -36 ≤ k ≤ 36, -10 ≤ l ≤ 6	
Reflections collected	11350	
Independent reflections	3708 [R(int) = 0.0252]	
Completeness to theta = 27.43°	99.9 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9817 and 0.9336	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3708 / 0 / 242	
Goodness-of-fit on F ²	1.065	
Final R indices [I > 2σ(I)]	R1 = 0.0491, wR2 = 0.1314	
R indices (all data)	R1 = 0.0620, wR2 = 0.1391	
Largest diff. peak and hole	0.337 and -0.211 e.Å ⁻³	

Crystal data and structure refinement for **2b**

Identification code	9177	
Empirical formula	C ₁₈ H ₁₈ N ₂ O ₈	
Formula weight	390.34	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.1282(4) Å	α = 90°.
	b = 25.3958(10) Å	β = 93.9020(10)°.
	c = 12.4272(5) Å	γ = 90°.
Volume	3503.9(2) Å ³	
Z	8	
Density (calculated)	1.480 Mg/m ³	
Absorption coefficient	0.118 mm ⁻¹	
F(000)	1632	
Crystal size	0.58 x 0.34 x 0.12 mm ³	
Theta range for data collection	1.83 to 27.50°.	
Index ranges	-10 ≤ h ≤ 14, -32 ≤ k ≤ 32, -16 ≤ l ≤ 14	
Reflections collected	24761	
Independent reflections	8027 [R(int) = 0.0234]	
Completeness to theta = 27.50°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9860 and 0.9346	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	8027 / 5 / 539	
Goodness-of-fit on F ²	1.050	
Final R indices [I > 2σ(I)]	R1 = 0.0457, wR2 = 0.1235	
R indices (all data)	R1 = 0.0548, wR2 = 0.1303	
Largest diff. peak and hole	0.322 and -0.246 e.Å ⁻³	

Crystal data and structure refinement for **2c**

Identification code	9180	
Empirical formula	C ₂₅ H ₃₂ N ₂ O ₈	
Formula weight	488.53	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.6807(5) Å	α = 80.749(2)°.
	b = 12.2715(8) Å	β = 73.924(2)°.
	c = 12.4359(8) Å	γ = 81.848(2)°.
Volume	1249.75(14) Å ³	
Z	2	
Density (calculated)	1.298 Mg/m ³	
Absorption coefficient	0.097 mm ⁻¹	
F(000)	520	
Crystal size	0.50 x 0.20 x 0.14 mm ³	
Theta range for data collection	1.69 to 27.50°.	
Index ranges	-11 ≤ h ≤ 10, -15 ≤ k ≤ 14, -16 ≤ l ≤ 12	
Reflections collected	8919	
Independent reflections	5693 [R(int) = 0.0188]	
Completeness to theta = 27.50°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9865 and 0.9531	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5693 / 8 / 346	
Goodness-of-fit on F ²	1.047	
Final R indices [I > 2σ(I)]	R1 = 0.0535, wR2 = 0.1438	
R indices (all data)	R1 = 0.0654, wR2 = 0.1525	
Largest diff. peak and hole	0.317 and -0.194 e.Å ⁻³	

Crystal data and structure refinement for **2d**

Identification code	7172	
Empirical formula	C ₁₉ H ₂₀ N ₂ O ₉	
Formula weight	420.37	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.4376(7) Å	α = 108.302(2)°.
	b = 11.7525(11) Å	β = 104.038(2)°.
	c = 12.3504(12) Å	γ = 100.220(2)°.
Volume	955.90(16) Å ³	
Z	2	
Density (calculated)	1.460 Mg/m ³	
Absorption coefficient	0.118 mm ⁻¹	
F(000)	440	
Crystal size	0.54 x 0.28 x 0.12 mm ³	
Theta range for data collection	1.83 to 27.49°.	
Index ranges	-9 ≤ h ≤ 9, -13 ≤ k ≤ 15, -16 ≤ l ≤ 13	
Reflections collected	6786	
Independent reflections	4383 [R(int) = 0.0250]	
Completeness to theta = 27.49°	99.4 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9860 and 0.9392	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4383 / 0 / 280	
Goodness-of-fit on F ²	1.048	
Final R indices [I > 2σ(I)]	R ₁ = 0.0550, wR ₂ = 0.1344	
R indices (all data)	R ₁ = 0.0808, wR ₂ = 0.1485	
Largest diff. peak and hole	0.294 and -0.272 e.Å ⁻³	

Crystal data and structure refinement for **3a**

Identification code	8010	
Empirical formula	C ₂₅ H ₂₃ N ₃ O ₉	
Formula weight	509.46	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 7.0390(6) Å	α = 90°.
	b = 24.783(2) Å	β = 100.260(2)°.
	c = 13.5449(12) Å	γ = 90°.
Volume	2325.1(3) Å ³	
Z	4	
Density (calculated)	1.455 Mg/m ³	
Absorption coefficient	0.112 mm ⁻¹	
F(000)	1064	
Crystal size	0.56 x 0.46 x 0.14 mm ³	
Theta range for data collection	1.64 to 27.43°.	
Index ranges	-8 ≤ h ≤ 9, -32 ≤ k ≤ 24, -17 ≤ l ≤ 17	
Reflections collected	16262	
Independent reflections	5293 [R(int) = 0.0307]	
Completeness to theta = 27.43°	99.8 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9844 and 0.9397	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5293 / 0 / 346	
Goodness-of-fit on F ²	1.062	
Final R indices [I > 2σ(I)]	R1 = 0.0493, wR2 = 0.1259	
R indices (all data)	R1 = 0.0671, wR2 = 0.1355	
Largest diff. peak and hole	0.739 and -0.532 e.Å ⁻³	

Crystal data and structure refinement for **3b**

Identification code	8533	
Empirical formula	C ₂₇ H ₂₇ N ₃ O ₁₁	
Formula weight	569.52	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.8202(4) Å	α = 102.7860(10)°.
	b = 11.1046(5) Å	β = 93.9600(10)°.
	c = 15.2948(7) Å	γ = 103.0680(10)°.
Volume	1251.77(10) Å ³	
Z	2	
Density (calculated)	1.511 Mg/m ³	
Absorption coefficient	0.119 mm ⁻¹	
F(000)	596	
Crystal size	0.60 x 0.30 x 0.20 mm ³	
Theta range for data collection	1.38 to 27.50°.	
Index ranges	-10 ≤ h ≤ 10, -14 ≤ k ≤ 14, -19 ≤ l ≤ 19	
Reflections collected	16471	
Independent reflections	5736 [R(int) = 0.0256]	
Completeness to theta = 27.50°	99.7 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9766 and 0.9321	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5736 / 0 / 384	
Goodness-of-fit on F ²	1.038	
Final R indices [I > 2σ(I)]	R1 = 0.0429, wR2 = 0.1146	
R indices (all data)	R1 = 0.0469, wR2 = 0.1176	
Largest diff. peak and hole	0.427 and -0.209 e.Å ⁻³	

Crystal data and structure refinement for **3c**

Identification code	8534	
Empirical formula	C ₂₈ H ₂₉ N ₃ O ₁₂	
Formula weight	599.54	
Temperature	295(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.6819(6) Å	α = 70.1970(10)°.
	b = 12.8663(9) Å	β = 84.768(2)°.
	c = 15.3441(11) Å	γ = 76.122(2)°.
Volume	1385.15(18) Å ³	
Z	2	
Density (calculated)	1.437 Mg/m ³	
Absorption coefficient	0.114 mm ⁻¹	
F(000)	628	
Crystal size	0.70 x 0.36 x 0.20 mm ³	
Theta range for data collection	1.41 to 27.50°.	
Index ranges	-9 ≤ h ≤ 9, -16 ≤ k ≤ 16, -19 ≤ l ≤ 19	
Reflections collected	18159	
Independent reflections	6348 [R(int) = 0.0315]	
Completeness to theta = 27.50°	99.9 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9776 and 0.9245	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6348 / 0 / 403	
Goodness-of-fit on F ²	1.017	
Final R indices [I > 2σ(I)]	R1 = 0.0559, wR2 = 0.1378	
R indices (all data)	R1 = 0.0765, wR2 = 0.1497	
Largest diff. peak and hole	0.284 and -0.249 e.Å ⁻³	

Crystal data and structure refinement for **3d**

Identification code	7322	
Empirical formula	C35 H43 N3 O12	
Formula weight	697.72	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.8316(8) Å	$\alpha = 83.062(2)^\circ$.
	b = 15.8889(18) Å	$\beta = 78.939(3)^\circ$.
	c = 16.4300(18) Å	$\gamma = 87.588(2)^\circ$.
Volume	1737.1(3) Å ³	
Z	2	
Density (calculated)	1.334 Mg/m ³	
Absorption coefficient	0.101 mm ⁻¹	
F(000)	740	
Crystal size	0.60 x 0.10 x 0.06 mm ³	
Theta range for data collection	1.70 to 25.00°.	
Index ranges	-8 ≤ h ≤ 8, -18 ≤ k ≤ 18, -19 ≤ l ≤ 19	
Reflections collected	18541	
Independent reflections	6122 [R(int) = 0.0451]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9940 and 0.9418	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6122 / 0 / 466	
Goodness-of-fit on F ²	1.121	
Final R indices [I > 2σ(I)]	R1 = 0.0643, wR2 = 0.1517	
R indices (all data)	R1 = 0.0840, wR2 = 0.1628	
Largest diff. peak and hole	0.286 and -0.258 e.Å ⁻³	

Crystal data and structure refinement for **4a**

Identification code	7562	
Empirical formula	C33 H30 N4 O11	
Formula weight	658.61	
Temperature	223(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.0316(10) Å	$\alpha = 109.279(2)^\circ$.
	b = 13.8306(17) Å	$\beta = 93.852(2)^\circ$.
	c = 15.0009(18) Å	$\gamma = 106.744(2)^\circ$.
Volume	1481.7(3) Å ³	
Z	2	
Density (calculated)	1.476 Mg/m ³	
Absorption coefficient	0.113 mm ⁻¹	
F(000)	688	
Crystal size	0.80 x 0.24 x 0.12 mm ³	
Theta range for data collection	1.46 to 27.49°.	
Index ranges	-10<= <i>h</i> <=10, -17<= <i>k</i> <=17, -19<= <i>l</i> <=19	
Reflections collected	10240	
Independent reflections	6769 [R(int) = 0.0303]	
Completeness to theta = 27.49°	99.4 %	
Absorption correction	Sadabs, (Sheldrick 2001)	
Max. and min. transmission	0.9866 and 0.9153	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6769 / 0 / 450	
Goodness-of-fit on F ²	1.002	
Final R indices [I>2sigma(I)]	R1 = 0.0616, wR2 = 0.1287	
R indices (all data)	R1 = 0.1030, wR2 = 0.1457	
Largest diff. peak and hole	0.497 and -0.298 e.Å ⁻³	